## Pending Claims in U.S. Application No. 09/776,936 (October 7, 2004):



# 1. A compound of formula I:

wherein A is

 $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are each, independently, H, halogen,  $NO_2$ ,

C<sub>1-10</sub>- alkyl, optionally substituted by halogen up to perhaloalkyl,

C<sub>1-10</sub>-alkoxy, optionally substituted by halogen up to perhaloalkoxy,

C<sub>1-10</sub>- alkanoyl, optionally substituted by halogen up to perhaloalkanoyl,

 $C_{6-12}$  aryl, optionally substituted by  $C_{1-10}$  alkyl or  $C_{1-10}$  alkoxy, or

 $C_{5-12}$  hetaryl, optionally substituted by  $C_{1-10}$  alkyl or  $C_{1-10}$  alkoxy,

and either

one of 
$$R^3$$
,  $R^4$ ,  $R^5$  and  $R^6$  is  $-M-L^1$ ; or

two adjacent of  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  together are an aryl or hetaryl ring with 5-12 atoms, optionally substituted by  $C_{1-10}$ -alkyl, , halo-substituted  $C_{1-10}$ -alkyl up to perhaloalkyl,

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 $C_{1-10}$ -alkoxy, halo-substituted  $C_{1-10}$ -alkoxy up to perhaloalkoxy,  $C_{3-10}$ -cycloalkyl,  $C_{2-10}$ -alkenyl,  $C_{1-10}$ -alkanoyl,  $C_{6-12}$ -aryl,  $C_{5-12}$ -hetaryl;  $C_{6-12}$ -aralkyl,  $C_{6-12}$ -alkaryl, halogen;  $NR^1R^1$ ;  $-NO_2$ ;  $-CF_3$ ;  $-COOR^1$ ;  $-NHCOR^1$ ; -CN;  $-CONR^1R^1$ ;  $-SO_2R^2$ ;  $-SOR^2$ ;  $-SR^2$ ; in which

 $R^1$  is H or  $C_{1-10}$ -alkyl, optionally substituted by halogen up to perhaloalkyl and  $R^2$  is  $C_{1-10}$ -alkyl, optionally substituted by halogen, up to perhaloalkyl,

R3', R4', R5' and R6' are independently H, halogen,

C<sub>1</sub> - C<sub>10</sub> alkyl, optionally substituted by halogen up to perhaloalkyl,

 $C_1$  – $C_{10}$  alkoxy optionally substituted by halogen up to perhaloalkoxy or two adjacent of  $R^{3'}$ ,  $R^{4'}$ ,  $R^{5'}$  and  $R^{6'}$ , together with the base phenyl, form a naphthyl group, optionally substituted by halogen up to perhalo,  $C_{1-10}$  alkyl,  $C_{1-10}$  alkoxy,  $C_{3-10}$  cycloalkyl,  $C_{2-10}$  alkenyl,  $C_{1-10}$  alkanoyl,  $C_{6-12}$  aryl,  $C_{5-12}$  hetaryl or  $C_{6-12}$  aralkyl;

M is  $-CH_2$ -, -S-,  $-N(CH_3)$ -, -NHC(O)-  $-CH_2$ -S-, -S- $-CH_2$ -, -C(O)-, or -O-; and

 $L^1$  is phenyl, substituted by  $C_{1-10}$ -alkoxy, OH, -SCH<sub>3</sub>, or by

pyridyl, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub>, or NO<sub>2</sub>, naphthyl, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyridone, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyrazine, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyrimidine, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, benzodioxane, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>,

benzopyridine, optionally substituted by  $C_{1-10}$ -alkyl, one  $C_{1-10}$ -alkoxy, halogen, -OH, -SCH<sub>3</sub> or NO<sub>2</sub>,

or

benzothiazole, optionally substituted by,  $C_{1-10}$  alkyl  $C_{1-10}$  alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, and wherein the compound of formula I has a pKa greater than 10,

or a pharmaceutically acceptable salt thereof.

#### 2. (Cancelled)

#### 3. A compound according to claim 1, wherein

R<sup>3</sup> is H, halogen or C<sub>1-10</sub>- alkyl, optionally substituted by halogen, up to perhaloalkyl;

R<sup>4</sup> is H, halogen or NO<sub>2</sub>;

 $R^5$  is H, halogen or  $C_{1-10}$ - alkyl;

R<sup>6</sup> is H, C<sub>1-10</sub>- alkoxy, thiophene, pyrole or methyl substituted pyrole,

 $R^{3'}$  is H, halogen,  $C_{4\text{-}10}$ -alkyl, or  $CF_3$  and

R<sup>6'</sup> is H, halogen, CH<sub>3</sub>, CF<sub>3</sub> or -OCH<sub>3</sub>.

#### 4. A compound according to claim 1, wherein

 $R^{3'}$  is  $C_{4-10}$ -alkyl, Cl, F or  $CF_3$ ;

R4' is H, Cl or F;

R<sup>5</sup>' is H, Cl, F or C<sub>4-10</sub>-alkyl; and

R<sup>6</sup>' is H or OCH<sub>3</sub>.

- 5. A compound according to claim 4, wherein R<sup>3</sup> or R<sup>5</sup> is t-butyl.
- 6. A compound according to claim 1, wherein M is  $-CH_2$ -,  $-N(CH_3)$  or -NHC(O)-.
  - 7. A compound according to claim 6, wherein  $L^1$  is phenyl or pyridyl.
  - 8. A compound according to claim 1, wherein M is -O-.
- 9. A compound according to claim 8, wherein  $L^1$  is phenyl, pyridyl, pyridone or benzothiazole.
  - 10. A compound according to claim 1, wherein M is -S-.
  - 11. A compound according to claim 10, wherein L<sup>1</sup> is phenyl or pyridyl.
  - 12. A compound of the formula

- 13. A pharmaceutical composition comprising a compound of claim 1, and a physiologically acceptable carrier.
- 14. A pharmaceutical composition comprising a compound of claim 12, and a physiologically acceptable carrier.
- 15. A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administering a compound of formula II:

or a pharmaceutically acceptable salt thereof wherein

A is

B is a substituted or unsubstituted, up to bicyclic aryl or heteroaryl moiety of up to 12 carbon atoms with at least one 6-member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is substituted it is substituted by one or more substituents selected from the group consisting of halogen, up to per-halo, and W<sub>n</sub>, wherein n is 0-3 and each W is independently selected from the group consisting of

-CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -C(O)-R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>1</sub>-C<sub>10</sub> alkenyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>6</sub>-C<sub>14</sub> aryl, optionally substituted with halogen, C<sub>1</sub>-C<sub>10</sub> alkyl, or C<sub>1</sub>-C<sub>10</sub> alkoxy; C<sub>7</sub>-C<sub>24</sub> alkaryl, optionally substituted with halogen, C<sub>1</sub>-C<sub>10</sub> alkyl, or C<sub>1</sub>-C<sub>10</sub> alkoxy; C<sub>3</sub>-C<sub>13</sub> heteroaryl, optionally substituted with halogen, C<sub>1</sub>-C<sub>10</sub> alkyl, or C<sub>1</sub>-C<sub>10</sub> alkoxy; C<sub>4</sub>-C<sub>23</sub> alkheteroaryl, optionally substituted with halogen, C<sub>1</sub>-C<sub>10</sub> alkyl, or C<sub>1</sub>-C<sub>10</sub> alkoxy; substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl and -M-L<sup>1</sup>;

wherein if W is a substituted group which does not contain aryl or hetaryl moieties, it is substituted by one or more substituents independently selected from the group consisting of -CN,  $-CO_2R^7$ ,  $-C(O)R^7$ ,  $-C(O)NR^7R^7$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $NO_2$ ,  $-NR^7C(O)R^7$ ,  $-NR^7C(O)OR^7$  and halogen up to per-halo;

wherein each R<sup>7</sup> is independently selected from H, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> hetaryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl, up to perhalosubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to perhalosubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl, up to perhalosubstituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, up to perhalosubstituted C<sub>6</sub>-C<sub>14</sub> aryl and up to perhalosubstituted C<sub>3</sub>-C<sub>13</sub> hetaryl,

wherein M is - O-, -S-, -N( $R^7$ )-, -(CH<sub>2</sub>)-m, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)mO-, -NR $^7$ C(O) NR $^7$ R $^7$ -, -NR $^7$ C(O)-, -C(O)NR $^7$ -, -(CH<sub>2</sub>)mS-, -(CH<sub>2</sub>)mN(R $^7$ )-, -O(CH<sub>2</sub>)m-, -CHX $^a$ , -CX $^a$ 2-, -S-(CH<sub>2</sub>)m- and -N(R $^7$ )(CH<sub>2</sub>)m-,

m = 1-3, and  $X^a$  is halogen; and

L¹ is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur, which is unsubstituted or substituted by halogen up to per-halo and optionally substituted by Z<sub>n1</sub>, wherein <sub>n1</sub> is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -C(O)-NR<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, - SR<sup>7</sup>, - NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -C(O)R<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> hetaryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl, substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, substituted C<sub>7</sub>-C<sub>24</sub> alkaryl and substituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl; wherein the one or more substituents of Z is selected from the group

consisting of -CN,  $-CO_2R^7$ ,  $-C(O)NR^7R^7$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NO_2$ ,  $-NR^7R^7$ ,  $-NR^7C(O)R^7$  and  $-NR^7C(O)OR^7$ ,

wherein  $R^{3'}$ ,  $R^{4'}$ ,  $R^{5'}$  and  $R^{6'}$  are each independently H, halogen,  $C_{1-10}$ -alkyl, optionally substituted by halogen up to perhaloalkyl,  $C_1$ – $C_{10}$  alkoxy, optionally substituted by halogen up to perhaloalkoxy or two adjacent of  $R^{3'}$ ,  $R^{4'}$ ,  $R^{5'}$  and  $R^{6'}$  together with the base phenyl, form a naphthyl group, optionally substituted by halogen up to perhalo,  $C_{1-10}$  alkyl,  $C_{1-10}$  alkoxy,  $C_{3-10}$  eycloalkyl,  $C_{2-10}$  alkenyl,  $C_{1-10}$  alkanoyl,  $C_{6-12}$  aryl,  $C_{5-12}$  hetaryl or  $C_{6-12}$  aralkyl.

16. A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administering a compound of formula IIa:

wherein A is

 $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are each independently H, halogen,  $NO_2$ ,  $C_{1-10}$ - alkyl, optionally substituted by halogen up to perhaloalkyl,  $C_{1-10}$ -alkoxy, optionally substituted by halogen up to perhaloalkoxy,  $C_{1-10}$ - alkanoyl, optionally substituted by halogen up to perhaloalkanoyl,  $C_{6-12}$  aryl, optionally substituted by  $C_{1-10}$  alkyl or  $C_{1-10}$  alkoxy, or

 $C_{5-12}$  hetaryl, optionally substituted by  $C_{1-10}$  alkyl or  $C_{1-10}$  alkoxy, and either

two adjacent of  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  together are an aryl or hetaryl ring with 5-12 atoms, optionally substituted by  $C_{1-10}$ -alkyl, halo-substituted  $C_{1-10}$ -alkyl up to perhaloalkyl,  $C_{1-10}$ -alkoxy, halo-substituted  $C_{1-10}$ -alkoxy up to perhaloalkoxy,  $C_{3-10}$ -cycloalkyl,  $C_{2-10}$ -alkenyl,  $C_{1-10}$ -alkanoyl;  $C_{6-12}$ -aryl,  $C_{5-12}$ -hetaryl,  $C_{6-12}$ -alkaryl, halogen; -NR<sup>1</sup>R<sup>1</sup>; -NO<sub>2</sub>; -CF<sub>3</sub>; COOR<sup>1</sup>; -NHCOR<sup>1</sup>; -CN; -CONR<sup>1</sup>R<sup>1</sup>; -SO<sub>2</sub>R<sup>2</sup>; -SOR<sup>2</sup>; -SR<sup>2</sup>;

in which

 $R^1$  is H or  $C_{1-10}$ -alkyl, optionally substituted by halogen, up to perhalo and

R<sup>2</sup> is C<sub>1-10</sub>-alkyl, optionally substituted by halogen,

R<sup>3'</sup>, R<sup>4'</sup>, R<sup>5'</sup> and R<sup>6'</sup> are independently H, halogen, C<sub>1</sub> - C<sub>10</sub> alkyl, optionally substituted by halogen up to perhaloalkyl, C<sub>1</sub> -C<sub>10</sub> alkoxy optionally substituted by halogen up to perhaloalkoxy or two adjacent of R<sup>3'</sup>, R<sup>4'</sup>, R<sup>5'</sup> and R<sup>6'</sup>, together with the base phenyl, form a naphthyl group optionally substituted by halogen up to perhalo, C<sub>1-10</sub> alkyl, C<sub>1-10</sub> alkoxy, C<sub>3-10</sub> cycloalkyl, C<sub>2-10</sub> alkenyl, C<sub>1-10</sub> alkanoyl, C<sub>6-12</sub> aryl, C<sub>5-12</sub> hetaryl or C<sub>6-12</sub> aralkyl, halogen up to perhalo;

M is -CH<sub>2</sub>-, -S-, -N(CH<sub>3</sub>)-, -NHC(O)- -CH<sub>2</sub>-S-, -S-CH<sub>2</sub>-, -C(O)-, or -O-; and

 $L^1$  is phenyl, pyridyl, naphthyl, pyridone, pyrazine, pyrimidine, benzodiaxane, benzopyridine or benzothiazole, each optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub>, NO<sub>2</sub> or, where Y is phenyl, by

or a pharmaceutically acceptable salt thereof.

# 17. A method according to claim 16, wherein

 $R^3$  is halogen or  $C_{1-10}$ - alkyl, optionally substituted by halogen, up to perhaloalkyl;

R<sup>4</sup> is H, halogen or NO<sub>2</sub>;

 $R^5$  is H, halogen or  $C_{1-10}$ - alkyl;

R<sup>6</sup> is H, C<sub>1-10</sub>- alkoxy, thiophene, pyrole or methylsubstituted pyrole

R<sup>3'</sup> is H, halogen, C<sub>4-10</sub>-alkyl, or CF<sub>3</sub> and

R<sup>6</sup> is H, halogen, CH<sub>3</sub>, CF<sub>3</sub> or OCH<sub>3</sub>.

- 18. A method according to claim 16, wherein M is -CH<sub>2</sub>-,-S-, -N(CH<sub>3</sub>)- or NHC(O)- and  $L^1$  is phenyl or pyridyl.
- 19. A method according to claim 16, wherein M is -O- and L<sup>1</sup> is phenyl, pyridone, pyrimidine, pyridyl or benzothiazole.

#### 20. A compound of formula I:

$$R^4$$
 $R^5$ 
 $R^6$ 
 $R^6$ 
 $R^6$ 
 $R^7$ 
 $R^8$ 
 $R^8$ 

wherein A is

 $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are each, independently, H, halogen,  $NO_2$ ,  $C_{1-10}$ - alkyl, optionally substituted by halogen up to perhaloalkyl,  $C_{1-10}$ -alkoxy, optionally substituted by halogen up to perhaloalkoxy, pyridinyl, optionally substituted by  $C_{1-10}$  alkyl or  $C_{1-10}$  alkoxy, and one of  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  is  $-M-L^1$ ;

 $R^{3'}$ ,  $R^{4'}$ ,  $R^{5'}$  and  $R^{6'}$  are independently H, halogen,  $C_1$  -  $C_{10}$  alkyl, optionally substituted by halogen up to perhaloalkyl,  $C_1$  - $C_{10}$  alkoxy optionally substituted by halogen up to perhaloalkoxy or two adjacent of  $R^{3'}$ ,  $R^{4'}$ ,  $R^{5'}$  and  $R^{6'}$ , together with the base phenyl, form a naphthyl group, optionally substituted by  $C_{1-10}$  alkyl,  $C_{1-10}$  alkoxy,  $C_{3-10}$  cycloalkyl,  $C_{2-10}$  alkenyl,  $C_{1-10}$  alkanoyl,  $C_{6-12}$  aryl,  $C_{5-12}$  hetaryl or  $C_{6-12}$  aralkyl;

 $R^{3'}$  is H, halogen,  $C_1$  -  $C_{10}$  alkyl, optionally substituted by halogen up to perhaloalkyl,  $C_1$ - $C_{10}$  alkoxy optionally substituted by halogen up to perhaloalkoxy

M is -CH<sub>2</sub>-, -S-, -N(CH<sub>3</sub>)-, -NHC(O)- -CH<sub>2</sub>-S-, -S-CH<sub>2</sub>-, -C(O)-, or -O-; and

 $L^1$  is phenyl, substituted by  $C_{1-10}$ -alkoxy, OH, -SCH<sub>3</sub>, or by

$$-$$

pyridyl, optionally substituted by C<sub>1-10</sub>-alkyl, C<sub>1-10</sub>-alkoxy, halogen, OH, -SCH<sub>3</sub>, or NO<sub>2</sub>,

naphthyl, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyridone, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyrazine, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyrimidine, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, benzodioxane, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>,

benzopyridine, optionally substituted by  $C_{1\text{--}10}$ -alkyl, OH, one  $C_{1\text{--}10}$ -alkoxy, halogen, -SCH<sub>3</sub> or NO<sub>2</sub>,

or

benzothiazole, optionally substituted by,  $C_{1-10}$  alkyl  $C_{1-10}$  alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, and wherein the compound of formula I has a pKa greater than 10, or a pharmaceutically acceptable salt thereof.

## 21. A compound of formula I:

$$R^4$$
 $R^5$ 
 $R^6$ 
 $NH$ 
 $NH$ 
 $NH$ 

wherein A is

wherein

 $R^3$  is H, halogen or  $C_{1-10}$ - alkyl, optionally substituted by halogen, up to perhaloalkyl;

R<sup>4</sup> is H, halogen or NO<sub>2</sub>;

 $R^5$  is H, halogen or  $C_{1-10}$ - alkyl;

R<sup>6</sup> is H, C<sub>1-10</sub>- alkoxy, thiophene, pyrole or methyl substituted pyrole,

R3' is H, Cl, F, C4-10-alkyl, or CF3 and

 $R^{4'}$  is H, Cl or F;

R<sup>5'</sup> is H, Cl, F or C<sub>4-10</sub>-alkyl; and

R<sup>6</sup> is H, halogen, CH<sub>3</sub>, CF<sub>3</sub> or -OCH<sub>3</sub>.

and one of R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> is -M-L<sup>1</sup>; wherein

M is  $-CH_2$ -, -S-,  $-N(CH_3)$ -, -NHC(O)-  $-CH_2$ -S-, -S- $-CH_2$ -, -C(O)-, or -O-; and

 $L^1$  is phenyl, substituted by  $C_{1-10}$ -alkoxy, OH, -SCH<sub>3</sub>, or by

$$-$$
N $\bigcirc$ 

pyridyl, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub>, or NO<sub>2</sub>, naphthyl, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>,

pyridone, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyrazine, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyrimidine, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, benzodioxane, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>,

benzopyridine, optionally substituted by  $C_{1-10}$ -alkyl, one  $C_{1-10}$ -alkoxy, halogen, -SCH<sub>3</sub> or NO<sub>2</sub>,

or

benzothiazole, optionally substituted by,  $C_{1^{-}10}$  alkyl  $C_{1^{-}10}$  alkoxy, halogen, -SCH<sub>3</sub> or NO<sub>2</sub>, and wherein the compound of formula I has a pKa greater than 10, or a pharmaceutically acceptable salt thereof.

- 22. A compound according to claim 21, wherein R<sup>3</sup> or R<sup>5</sup> is t-butyl.
- 23. A compound according to claim 21, wherein M is  $-CH_2$ -,  $-N(CH_3)$  or -NHC(O)-.
  - 24. A compound according to claim 21, wherein  $L^1$  is phenyl or pyridyl.
  - 25. A compound according to claim 21, wherein M is -S-.
  - 26. A compound according to claim 26, wherein  $L^1$  is phenyl or pyridyl.

## 27. A compound of formula I:

wherein A is

R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are each, independently, H, halogen, NO<sub>2</sub>,

 $C_{1\text{--}10}$ - alkyl, optionally substituted by halogen up to perhaloalkyl,  $C_{1\text{--}10}$ -alkoxy, optionally substituted by halogen up to perhaloalkoxy,  $C_{1\text{--}10}$ - alkanoyl, optionally substituted by halogen up to perhaloalkanoyl,  $C_{6\text{--}12}$  aryl, optionally substituted by  $C_{1\text{--}10}$  alkyl or  $C_{1\text{--}10}$  alkoxy, or  $C_{5\text{--}12}$  hetaryl, optionally substituted by  $C_{1\text{--}10}$  alkyl or  $C_{1\text{--}10}$  alkoxy, and either

one of  $R^3$ ,  $R^4$ , and  $R^5$  is  $-M-L^1$ ; or

two adjacent of  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  together are an aryl or hetaryl ring with 5-12 atoms, optionally substituted by  $C_{1\text{-}10}$ -alkyl, , halo-substituted  $C_{1\text{-}10}$ -alkyl up to perhaloalkyl,  $C_{1\text{-}10}$ -alkoxy, halo-substituted  $C_{1\text{-}10}$ -alkoxy up to perhaloalkoxy,  $C_{3\text{-}10}$ -cycloalkyl,  $C_{2\text{-}10}$ -

alkenyl,  $C_{1-10}$ -alkanoyl,  $C_{6-12}$ -aryl,  $C_{5-12}$ -hetaryl;  $C_{6-12}$ -aralkyl,  $C_{6-12}$ -alkaryl, halogen;  $NR^1R^1$ ; -NO<sub>2</sub>; -CF<sub>3</sub>; -COOR<sup>1</sup>; -NHCOR<sup>1</sup>; -CN; -CONR<sup>1</sup>R<sup>1</sup>; -SO<sub>2</sub>R<sup>2</sup>; -SOR<sup>2</sup>; -SR<sup>2</sup>; in which

 $R^1$  is H or  $C_{1-10}$ -alkyl, optionally substituted by halogen up to perhaloalkyl and  $R^2$  is  $C_{1-10}$ -alkyl, optionally substituted by halogen, up to perhaloalkyl,

R<sup>3'</sup>, R<sup>4'</sup>, R<sup>5'</sup> and R<sup>6'</sup> are independently H, halogen,

C<sub>1</sub> - C<sub>10</sub> alkyl, optionally substituted by halogen up to perhaloalkyl,

 $C_1$  – $C_{10}$  alkoxy optionally substituted by halogen up to perhaloalkoxy or two adjacent of  $R^{3'}$ ,  $R^{4'}$ ,  $R^{5'}$  and  $R^{6'}$ , together with the base phenyl, form a naphthyl group, optionally substituted by halogen up to perhalo,  $C_{1-10}$  alkyl,  $C_{1-10}$  alkoxy,  $C_{3-10}$  cycloalkyl,  $C_{2-10}$  alkenyl,  $C_{1-10}$  alkanoyl,  $C_{6-12}$  aryl,  $C_{5-12}$  hetaryl or  $C_{6-12}$  aralkyl;

M is  $-CH_2$ -, -S-,  $-N(CH_3)$ -, -NHC(O)-  $-CH_2$ -S-, -S- $-CH_2$ -, -C(O)-, or -O-; and

 $L^1$  is phenyl, substituted by  $C_{1-10}$ -alkoxy, OH, -SCH<sub>3</sub>, or by

$$-$$
N $\bigcirc$ 

pyridyl, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub>, or NO<sub>2</sub>, naphthyl, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyridone, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyrazine, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, pyrimidine, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, benzodioxane, optionally substituted by  $C_{1-10}$ -alkyl,  $C_{1-10}$ -alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>,

benzopyridine, optionally substituted by  $C_{1\text{--}10}\text{--alkyl},$  one  $C_{1\text{--}10}\text{--alkoxy},$  halogen, OH,  $\,\text{--SCH}_3$  or  $NO_2$  ,

or

benzothiazole, optionally substituted by,  $C_{1-10}$  alkyl  $C_{1-10}$  alkoxy, halogen, OH, -SCH<sub>3</sub> or NO<sub>2</sub>, or a pharmaceutically acceptable salt thereof.